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Extended-spectrum beta-lactamase in *Escherichia coli* isolated from humans, animals, and environments in Bangladesh: A One Health perspective systematic review and meta-analysis

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ABSTRACT

Extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* has been linked to both life-threatening hospital- and community-acquired infections across the globe. Here, we conducted a systematic review and meta-analysis to evaluate the prevalence of ESBL in *E. coli* isolated from humans, animals, and environments in Bangladesh. Following the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines, the current systematic review and meta-analysis was taken into account for studies published between 2010 and 2021 in peer-reviewed journals. The meta-analysis was performed on "R" version 4.2.2. A total of 36 studies were included in this systematic review and meta-analysis; among them, 22 were human, seven were animal, four were environmental, and three were multidisciplinary studies. The meta-analysis revealed that the pooled prevalence of ESBL-producing *E. coli* in Bangladesh was 21% (95% CI: 15%–27%). On the sample basis, the pooled prevalence of ESBL-producing *E. coli* in humans, animals, and environments was 17% (95% CI: 11%–23%), 22% (95% CI: 9%–34%), and 39% (95% CI: 16%–62%), respectively. All the pooled prevalence of ESBL-producing *E. coli* showed substantial heterogeneity ($I^2 > 75\%$; $p < 0.05$) among the selected studies. This systematic review reported 13 different types of resistance genes encoding ESBL, such as bla_{TEM-1} (37.5%), bla_{CMY} (34.6%), $bla_{CTX-M-1}$ (20.7%), $bla_{CTX-M-15}$ (16.1%), bla_{TEM} (12.3%), bla_{CTX-M} and bla_{OXA} (9.6%), bla_{OXA-1} (5.8%), bla_{ampC} (3.9%), bla_{SHV} (3.8%), bla_{CMY-2} (2.3%), $bla_{CTX-M-14}$ (1.3%), and $bla_{CTX-M-9}$ (0.3%). Moreover, 39 types of epidemiologically important clones (including ST10 and ST131) were detected in ESBL-producing *E. coli* isolated from humans, animals, and environments in Bangladesh. To the best of our knowledge, this is the first systematic review and meta-analysis of integrated studies on ESBL-producing *E. coli* using the One Health approach in Bangladesh. The high prevalence of ESBL-producing *E. coli*, their resistance genes, and epidemiologically important clones in humans, animals, and environments highlights the importance of implementing comprehensive antimicrobial resistance (AMR) surveillance under a One Health perspective to mitigate the AMR consequences in Bangladesh.

1. Introduction

As a major threat to public health, antimicrobial resistance (AMR) reduces the effectiveness of currently available antibiotic treatments for bacterial infections. Due to the ecological niche between patients, antimicrobial exposure, and hospital-adaptation, AMR microbes are commonly found in healthcare facilities [1]. The health of humans, animals, and environments is threatened by the consequences of AMR [2]. Moreover, it is abundantly obvious that AMR in livestock is intricately connected to their existence in humans and environments as well [3]. It is predicted that AMR would result in a significant number of deaths throughout the world [4]. It would also cause massive economic damages and a considerable drop in animal production globally [5].

In both humans and animals, *Escherichia coli* is one of the most common pathogens responsible for a wide variety of common bacterial diseases. Most of the cases, *E. coli* typically exists in the gut microbiota, but some *E. coli* strains are responsible for various severe infections, such as colibacillosis in poultry; mastitis in dairy cattle; urinary tract infection, neonatal meningitis, septicemia, etc. in humans [6,7]. This organism is also capable to develop more devastating effects because of its

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zoonotic characteristics [8]. Moreover, *E. coli* pathogen has the opportunity to be transferred to environmental settings from humans and animals.

It has been observed that the prevalence of AMR in *E. coli* has skyrocketed during the past several years [9]. Most commonly, bacteria produce beta-lactamase enzymes, which, by hydrolyzing the beta-lactam ring, can render the antibiotic ineffective [10]. The fast spread of enzyme-mediated resistance and the resulting rise of multidrug-resistant bacteria have earned it recognition as a global public health problem [11]. Extended-spectrum beta-lactamase (ESBL)-generating *E. coli* has emerged as a major health threat in both humans and animals. Since beta-lactam antibiotics are extensively used, *E. coli* has become resistant, resulting in widespread diseases in the community [12,13]. Infections generated by ESBL-producing *E. coli* pose a significant threat to healthcare settings because of the scarcity of effective empiric treatments [9].

The CTX-M, TEM, and SHV types of enzymes are the core components of ESBL and can be found in a wide variety of pathogens that are considered to be clinically significant around the world [14]. The majority of TEM and SHV types are thought to have originated from parent enzymes such as TEM-1, TEM-2, and SHV-1. This evolution occurred as a result of point mutations that occurred along the active sites of TEM and SHV sequences, which led to an increased spectrum of activity [9,15]. Moreover, there are around 220 different enzyme versions of CTX-M-lactamases. These enzymes are grouped together into five distinct groups, some of which are CTX-M-1, 2, 8, 9, and 25 [16]. Worldwide, ESBLs of the TEM, CTX-M, SHV, and OXA kinds have been reported often in *E. coli* isolated from humans, environments, animals, and foods derived from animals [17–21].

Widespread reports indicate that excessive and maybe inappropriate use of a variety of antibiotics is a major contributor to the spread of AMR in Bangladesh. The presence of ESBL-producing *E. coli* in humans, animals, and environments is a public health concern. Moreover, it is important to keep up-to-date data on ESBL-producing *E. coli* in health systems to minimize the consequences of ESBL-producers. In this study, we conducted a systematic review and meta-analysis on the current status of ESBL-producing *E. coli* in Bangladesh, taking into account studies conducted in humans, animals, and environments, in order to provide a detailed description and up-to-date information for professionals in a variety of fields.

2. Materials and methods

2.1. Review protocols

The review followed the guidelines for systematic reviews found in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [22]. The review followed the procedures outlined in the PRISMA statement, which included (1) searching database systems for potentially pertinent articles; (2) determining the extent to which the articles are acceptable to the review; (3) assessing the relevancy of the articles; and (4) extracting, screening, and analyzing the data. The protocol was established before starting the meta-analysis.

2.2. Search protocols

We took a rigorous approach to finding original scientific articles that were published between January 2010 and December 2021 and discussed the occurrence and distribution of ESBL-producing *E. coli* in Bangladesh. We used several database systems, including PubMed, ScienceDirect, Web of Science, BanglaJol, Scopus, Google Scholar, ResearchGate, EMBASE, and Crossref, to conduct a comprehensive literature search. Search terms we used include: “Bangladesh”, “*Escherichia coli*”, “*E. coli*”, “*Enterobacteriaceae*”, “extended-spectrum beta-lactamase”, “extended-spectrum-beta-lactamase”, “extended-spectrum β-lactamase”, “extended-spectrum-β-lactamase”, “ESBL”, “ESBLs”, “double-disk synergy test”, “humans”, “animals”, “environments”, “TEM”, “CTX-M", “SHV”, “CMY”, “OXA”, “AMPc”, and “STs clones”. According to the study’s objectives, a list of Boolean keywords was developed, including “AND” (for words in the same category) and “OR” (for words within a category). In addition to this, the reference lists of the articles that were chosen for further examination were provided in order to maximize the likelihood of acquiring other articles. During the survey, we downloaded articles directly from the journals or with the help of the Bangladesh Agricultural University Library Network (http://catalog.bau.edu.bd). The analysis included all articles that were eligible for inclusion. Two investigators (MS Islam and MT Rahman) performed all of the literature searches. All the authors re-examined the sources of all articles according to the international standards for systematic review.

2.3. Study inclusion and exclusion criteria

All the retrieved articles were verified before being included in the systematic review and meta-analysis. All the research articles that met the following standards were eligible for our systematic review and meta-analysis:

- Only those articles that focused on ESBL-producing *E. coli* isolated from human, animal, and environmental samples.
- Only those articles that had information on the sample size, total number of *E. coli* isolates, and total number of ESBL-producing *E. coli* isolates were included.
- Only those articles that were peer-reviewed and published between January 2010 and December 2021 were included.
- All the articles narrating the prevalence, occurrence, or characterization of ESBL-producing *E. coli* using both phenotypic and genotypic approaches.

The following criteria were used to compile the final list of articles. Articles were excluded from consideration if they met any one of the following criteria: (1) they were duplicates that had already been checked and dismissed; (2) they did not meet the inclusion criteria established; (3) they did not fall within the purview of our study; (4) they were published before 2010; (4) they were unavailable in full-text, or have only title and/or abstract; (5) they were unpublished, review articles or meta-analysis, conference or meeting abstracts.

2.4. Data extraction

Two authors (MS Islam and MT Rahman) took the initiative of going through the entire texts of the studies, taking into account the criteria for study eligibility, extracting reasonable data, and then entering the data into a spreadsheet. The other reviewers (AMMT Rahman and J Hassan) then double-checked these data. The data we extracted include the citation or title of the study, the name of the first author, the published year (2010−21), the study areas (districts), the study period, the sample categories and types, the sample size, the total number or prevalence of *E. coli* isolates, the total number or prevalence of ESBL-producing *E. coli* with their detection method (phenotypic and/or genotypic), the types of ESBL-encoding genes with their number or percentage, and the sequencing types of the isolates.

2.5. Statistical analysis

To perform data analysis, all the retrieved data were first imported into Excel-365 (Microsoft/Office 365, Redmond, WA, USA) and subsequently exported to R (version 4.2.2, The R Foundation for Statistical Computing, Vienna, Austria) and GraphPad Prism (version 8.4.2, GraphPad Software, CA, USA) after sorting the data.

The meta-analysis was carried out in RStudio.v.2022.07.2 + 576 by utilizing the “metaprop” codes that are included in the meta (version

6.0–0) package [23] of the R program. We used the residual maximum likelihood approach for the random-effects model to compute the pooled prevalence and 95% confidence interval (CI) of ESBL-producing *E. coli* isolated from humans, animals, and environments in Bangladesh. The statistical heterogeneity that existed between the studies was examined with the help of the Cochran's Q test for the significance of heterogeneity and the inconsistency index (I^2), where an I^2 value of >75% and a significance level of <0.05 (*p*-value) were considered to indicate a significant statistical variation [24]. Forest plots were prepared using the "forest" codes in the meta package, and images were extracted from the "R" plot using the "jpeg" and "dev.off()" codes. In addition, following the Wilson/Brown Hybrid technique [25], the GraphPad Prism was used to compute the prevalence and 95% CI of ESBLs encoding genes in *E. coli* isolated from humans, animals, and environments.

The author, MS Islam, performed all the analyses.

3. Results

3.1. Details of the included studies

Following the PRISMA guidelines, a total of 3065 articles (3013 articles found in the selected database and 52 in other sources) were included for the initial screening. After removing duplicate articles and articles that deviated from the concept of the review or lacked details, 94 articles were selected for eligibility evaluation. Finally, a total of 36 scientific articles fulfilled the eligibility criteria to be included in our present systematic review and meta-analysis (Fig. 1).

The study period of the selected articles was between 2003 and 2020, and the published period was between 2010 and 2021. Two articles [26,27] didn't mention the study period. Area-wise, these selected articles covered different districts of Bangladesh, among them, the highest studies were conducted in Dhaka district (21/36), followed by Rajshahi, Mymensingh, Sylhet, and Chottogram. Since both sample materials and scientific facilities were readily available in these regions, the majority of the studies were carried out there. These investigations were carried out in either a single district of Bangladesh or a cluster of districts. Amin et al. [28] conducted their study on samples collected from different districts of Bangladesh (Table 1).

3.2. Methods detecting ESBLs

Twelve out of 36 studies used a phenotypic assay to detect ESBL-producing *E. coli* from human, animal, and environmental samples. Most laboratories employ one of three methods to identify bacteria: disc diffusion (double disc synergy test), minimum inhibitory concentration (MIC), or the VITEK system. Moreover, four studies employed genotypic assays (especially polymerase chain reaction assay), and the remaining 20 articles used both phenotypic and genotypic approaches to identify ESBL-producing *E. coli* (Table 1).

3.3. Study categories

The selected studies were categorized into three classes based on the sample origin: humans, animals, and environments. >60% (22/36) of the studies focused on human samples, followed by animal (19.4%, 7/36) and environmental (11.1%, 4/36) samples. Moreover, three (8.3%) were multidisciplinary studies, analyzing samples collected from two or three categories at the same time. Different types of animals were under consideration for sub-classification of animal samples, including chickens (broilers, layers, cockerels, and sonali), wild birds, ducks, geese, pigeons, and cattle. It is worth noting that several different species of farm animals were examined in certain published works. In addition to sample categories, sample types include urine, different wound swabs, pus, sputum, exudates, swabs from vagina, nasopharynx, and throat, stool, and blood (humans), feces, cloacal swabs, meat, and meat swabs (animals), and water from different sources, fecal sludge, soil, and dirt (environments). Moreover, studies were conducted on a total of 8054 samples, where 70.6% ($n = 5686$), 19.2% ($n = 1549$), and 10.2% ($n = 819$) of the samples were collected from humans, animals, and environments, respectively (Table 1).

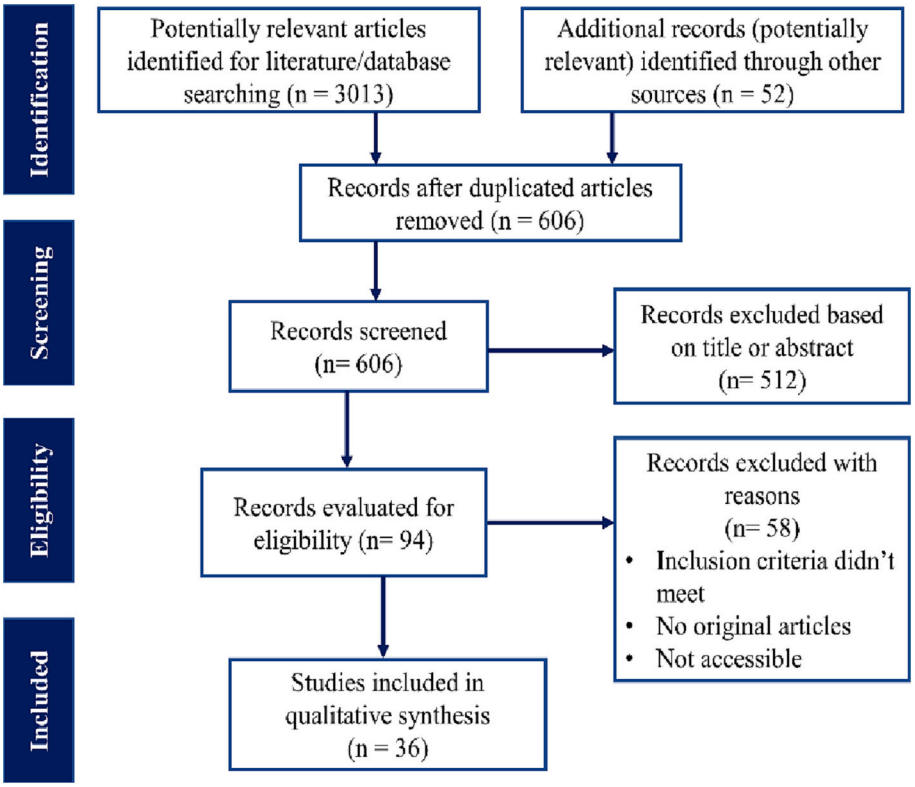

Fig. 1. A PRISMA flow diagram illustrating the process of selecting studies. We looked through several world-recognized online databases to find qualifying studies that reported ESBL-producing *E. coli,* and then we used predetermined search algorithms to find those studies. After combining the records and removing duplicates with the help of the Zotero software, the data were subjected to a screening based on the previously established eligibility criteria before being included in the systematic review and meta-analysis.

Table 1
Overall outcomes of studies published between 2010 and 2021 focusing ESBL-producing *E. coli* in humans, animals, and environments in Bangladesh.

Study area	Study Period	Published year	Sample categories	Sample types (N)	No. of *E. coli*	No. of ESBL-producers	ESBL detection method	Genes encoding ESBL	STs	References
Rajshahi	2008	2010	Humans	Wound swabs (125)	19	11	DD	–	–	[29]
Rajshahi	2009	2012	Wild ducks, ducks, chickens, geese	Cloacal swabs, feces (96)	66	36	DD, PCR	CTX-M1,9,14,15	√	[30]
Dhaka	2008–09	2013	Environments	Water (4)	4	2	DD	–	–	[31]
Dhaka	2010–11	2013	Humans	Wound swabs, urine (320)	90	29	DD, PCR	CTM-M, OXA	–	[32]
Dhaka	2010–11	2013	Humans	Urine, pus, sputum, swabs (200)	114	61	DD	–	–	[33]
Chattogram	2010	2014	Gull	Feces (150)	85	29	DD, PCR	CTX-M14,15	√	[34]
Cox's Bazar, Rangamati, Chattogram	2011	2014	Pigeons	Cloacal swabs (150)	36	7	DD, PCR	CTX-M15	√	[35]
Dhaka	2011–12	2014	Humans	Urine (300)	112	36	DD	–	–	[36]
Dhaka, Sylhet	2003–07	2014	Humans	Urine, surgical wound swab (339)	339	40	DD, PCR	TEM, CTX-M1,15, OXA1	–	[37]
Dhaka	NM	2014	Humans	Urine (44)	13	7	DD		–	[26]
Dhaka	2011	2014	Humans	Urine, pus, wound swab (354)	120	50	DD, PCR	SHV	–	[38]
Mymensingh	2011	2014	Humans	Urine, skin wound swabs (300)	156	35	DD, PCR	TEM, CTX-M, SHV	–	[39]
Dhaka	2005	2015	Humans	Urine (250)	69	22	DD	–	–	[40]
Dhaka, Moulavibazar, Sylhet, Rajshahi	2010	2015	Open Bill Stork, Environment	Feces, river water (170 + 8)	76 + 8	2 + 4	DD, PCR	CTX-M15	√	[41]
Mymensingh	2011	2015	Humans	Wound swab, pus (84)	39	24	DD	–	–	[42]
Dhaka	2014	2016	Humans	Urine (800)	90	34	DD, PCR	CTX-M15, OXA1	√	[43]
Dhaka	2006–07	2016	Humans	Pus, swab, exudates (125)	61	6	DD, PCR	TEM, CTX-M1, SHV, OXA	–	[44]
Dhaka	2012	2016	Humans, Poultry	Urine, feces (48 + 40)	14 + 11	11 + 11	DD, PCR	TEM, CTX-M, OXA	–	[45]
Dhaka	2016	2018	Humans	Urine (220)	103	23	DD		–	[46]
Mymensingh	2014–15	2018	Humans	Urine, pus, swab of wound, vaginal, throat (375)	233	100	PCR	TEM1, CTX-M1,9, SHV, AMPc	√	[47]
Tangail	2016	2018	Humans, chickens, cattle, Environments	stool, feces, soil/dirt (52 + 104 + 52)	50 + 102 + 23	3 + 2 + 2	DD, PCR	TEM, CTX-M, OXA1	–	[48]
Dhaka	2006	2018	Humans	surgical and burn wound (182)	45	17	DD	–	–	[49]
Chandpur	2017	2019	Humans	Stool (100)	82	74	DD, PCR	TEM, CTX-M1, OXA1	–	[50]
Dhaka, Bogura	2014	2019	Environments	Fecal sludge (34)	26	22	DD, PCR	TEM, CTX-M, OXA	–	[51]
Dhaka	2014	2019	Humans	Urine (200)	89	23	DD	–	–	[52]
Dhaka	2012	2019	Humans	Urine (90)	41	13	DD, PCR	TEM, CTX-M	–	[53]
Dhaka	NM	2019	Humans	Urine (59)	45	18	DD, PCR	CTX-M, SHV, OXA1, AMPc	–	[27]
Cox's Bazar	2018	2020	Environments	Water (421)	384	66	DD, PCR	TEM, CTX-M1,15	–	[54]
Dhaka, Sylhet, Mymensingh, Chattogram, Rajshahi	2019	2020	Broilers, cockerel	Meat (113)	86	74	DD, PCR	TEM	–	[55]
Sylhet, Moulavibazar, Sunamganj, Habiganj	2020	2020	Broilers, layers	Meat swabs (600)	381	53	PCR	SHV	–	[56]
Sirajganj	2020	2021	Humans	Urine (589)	127	103	DD	–	–	[57]
Different districts	2017–18	2021	Poultry Environments	Water (300)	300	183	DD, PCR	TEM, CTX-M1, SHV, CMY2, OXA1	–	[28]
Dhaka	2019	2021	Humans	Urine, sputum (100)	100	25	PCR	TEM, CTX-M15, SHV, OXA, AMPc	√	[58]
Rajshahi	2020	2021	Broilers, Layers, Sonali	Cloacal swabs (60)	37	13	DD	–	–	[59]
Dhaka	2015–19	2021	Humans	Nasopharyngeal swab, wound swab, stool, blood (430)	85	26	PCR	TEM	–	[60]
Magura	2019–20	2021	Migratory birds	Feces (66)	55	21	DD, PCR	TEM, CTX-M, SHV, CMY	–	[61]

Here, N = Sample size, ESBL = Extended-spectrum beta-lactamase, STs = Sequence types, DD = Disk diffusion method, PCR = Polymerase chain reaction, NM = Not mentioned.

3.4. Prevalence of E. coli

The total number of pooled *E. coli* isolates was 3916, where 2247 (57.4%), 935 (23.9%), and 734 (18.7%) of the isolates were identified in humans, animals, and environmental samples, respectively. According to the meta-analysis, the overall pooled prevalence of *E. coli* in the selected 36 scientific articles was 55% (95% CI: 46%–63%) with perfect heterogeneity ($I^2 = 100\%$, $p < 0.001$). Overall, the lowest and highest estimated prevalence of *E. coli* were 11% (95% CI: 9%–14%) and 100% (99%–100%), respectively. Sample-wise, the maximum and minimum prevalence of *E. coli* in human samples were 11% (95% CI: 9%–14%) and 100% (99%–100%), respectively; 24% (95% CI: 14%–32%) and 83% (95% CI: 72%–91%) in animal samples; and 76% (95% CI: 59%–89%) and 100% (95% CI: 99%–100%) in environmental samples, respectively (Fig. 2 and Table 1).

3.5. Distribution of ESBL-producing E. coli

In total, the pooled number of ESBL-producing *E. coli* isolates was 1318 (isolated from 8054 samples), revealing a pooled prevalence of 21% (95% CI: 15%–27%). The pooled prevalence of ESBL-producing *E. coli* isolates among different selected studies showed significant

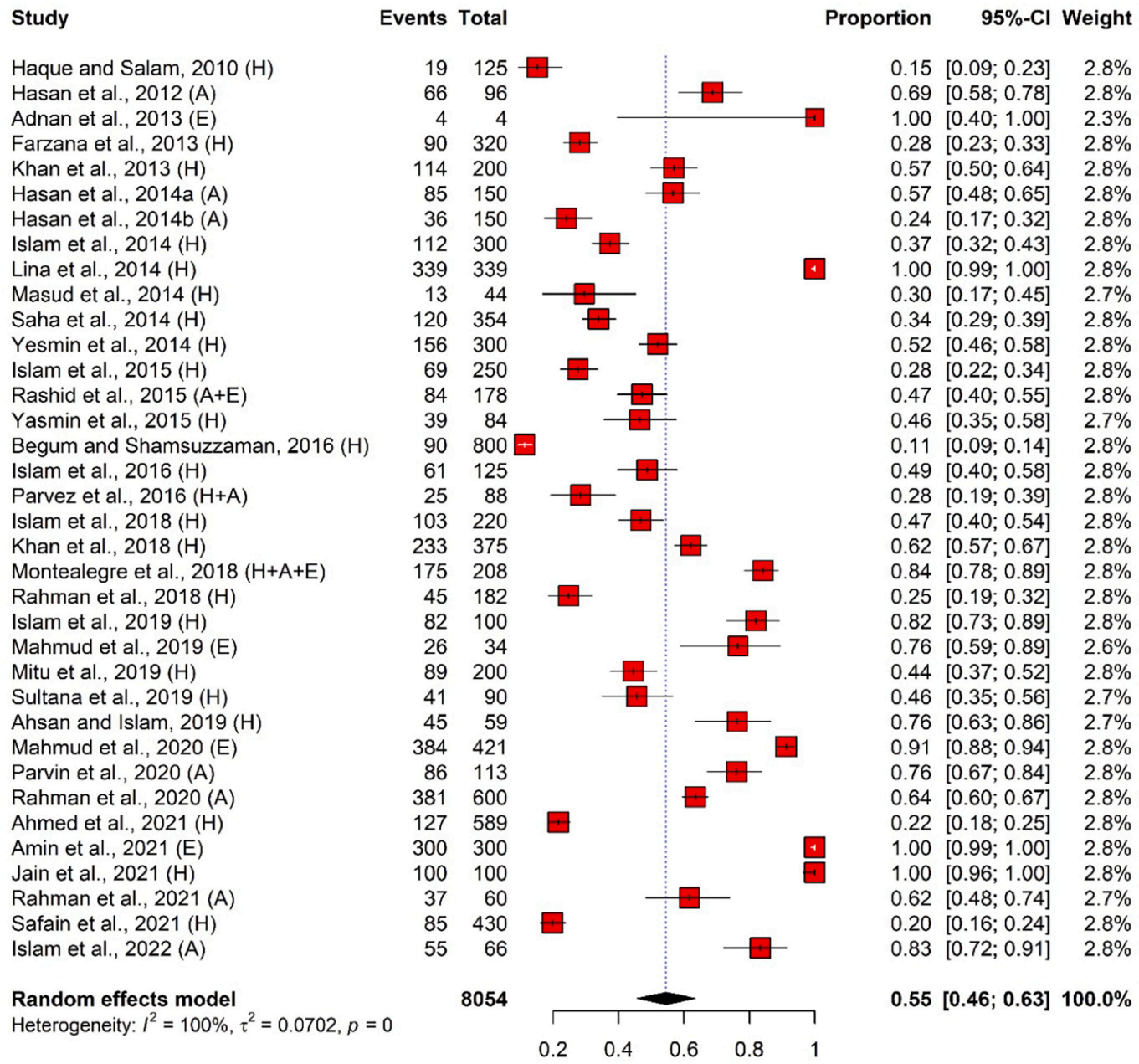

Fig. 2. Forest plot depicting the prevalence of *E. coli* isolated from humans, animals, and environments in Bangladesh. The estimate of the prevalence was determined by combining the findings of 36 separate studies by applying a random-effects model to the data. An I^2 value > 75% and a *p*-value < 0.05 were deemed statistically significant. The R program was used to analyse the data and generate the figure. Events = No. of positive *E. coli* isolated from each study, Total = Sample size of each study, CI = Confidence interval, H = Human, A = Animal, E = Environment.

heterogeneity (I^2 = 97%, p < 0.01). Overall, the highest and lowest prevalence of ESBL-producing *E. coli* isolated from humans, animals, and environments was 3% (95% CI: 1%–7%) and 74% (95% CI: 64%–82%) (Fig. 3).

3.5.1. Studies focusing humans

In human samples, the overall pooled number of ESBL-producing *E. coli* isolates was 791 (out of 5686 samples), and the pooled prevalence was 17% (95% CI: 11%–23%), with considerable heterogeneity (I^2 = 95%, p < 0.01). In total, the prevalence of ESBL-producing *E. coli* in human samples ranged from 4% (95% CI: 3%–6%) to 74% (95% CI: 64%–82%) (Fig. 4).

3.5.2. Studies focusing animals

Overall, 248 ESBL-producing *E. coli* isolates were detected in 1549 animal samples, and the pooled prevalence was 22% (95% CI: 9%–34%), with evidence of notable heterogeneity (I^2 = 97%, p < 0.01) among the selected 36 studies. In total, the highest prevalence of ESBL-producing *E. coli* was detected in a study (65%, 95% CI: 56%–74%) which was conducted in 2020, whereas the lowest prevalence was detected in a study (1%, 95% CI: 0%–4%) which was carried out in 2015 (Fig. 5).

3.5.3. Studies focusing environments

In environmental samples, the overall pooled number of ESBL-producing *E. coli* isolates was 279 (out of 819 samples), and the pooled prevalence was 39% (95% CI: 16%–62%), with substantial heterogeneity (I^2 = 98%, p < 0.01). In total, the prevalence of ESBL-

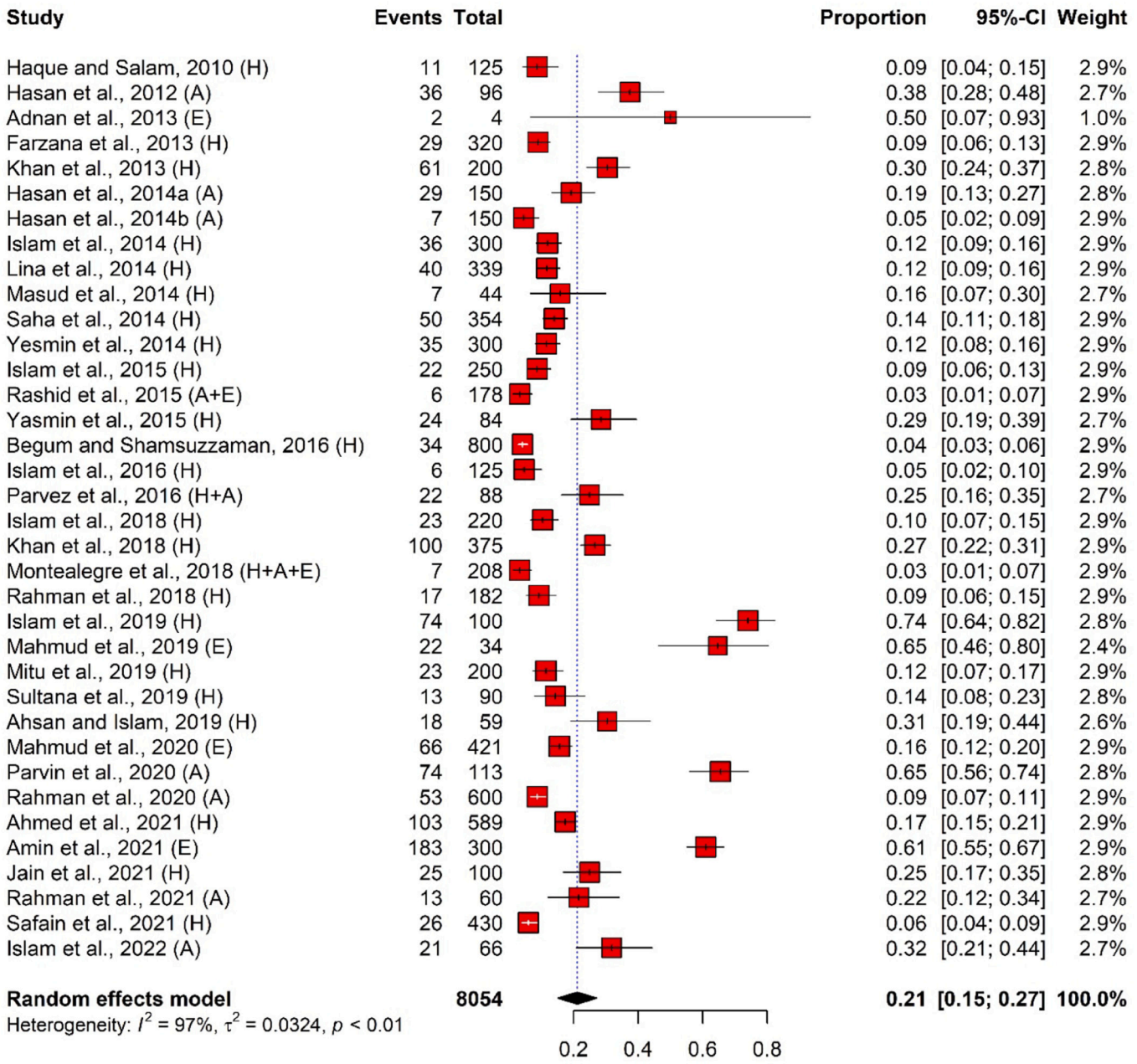

Fig. 3. Forest plot depicting the prevalence of ESBL-producing *E. coli* isolated from One Health components in Bangladesh. The estimate of the prevalence was determined by combining the findings of 36 separate studies by applying a random-effects model to the data. An I^2 value > 75% and a p-value < 0.05 were deemed statistically significant. The R program was used to analyse the data and generate the figure. Events = No. of positive ESBL-producing *E. coli* isolated from each study, Total = Sample size of each study, CI = Confidence interval, H = Human, A = Animal, E = Environment.

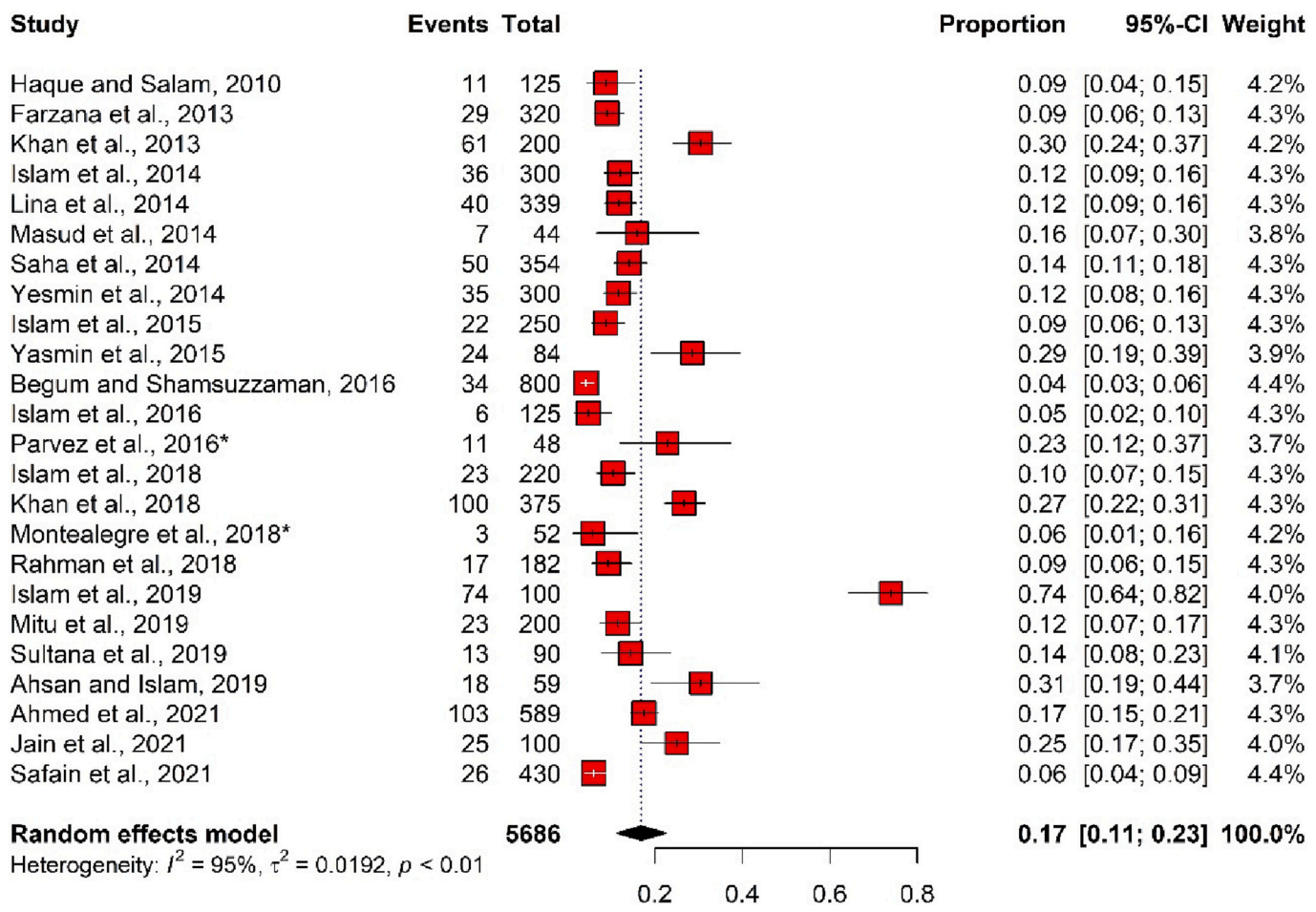

Fig. 4. Forest plot depicting the prevalence of ESBL-producing *E. coli* isolated from human samples in Bangladesh. The estimate of the prevalence was determined by combining the findings of 22 separate studies by applying a random-effects model to the data. An I^2 value > 75% and a p-value < 0.05 were deemed statistically significant. The R program was used to analyse the data and generate the figure. Events = No. of positive ESBL-producing *E. coli* isolated from each study, Total = Sample size of each study, CI = Confidence interval, * = Study conducted with more than one sample category.

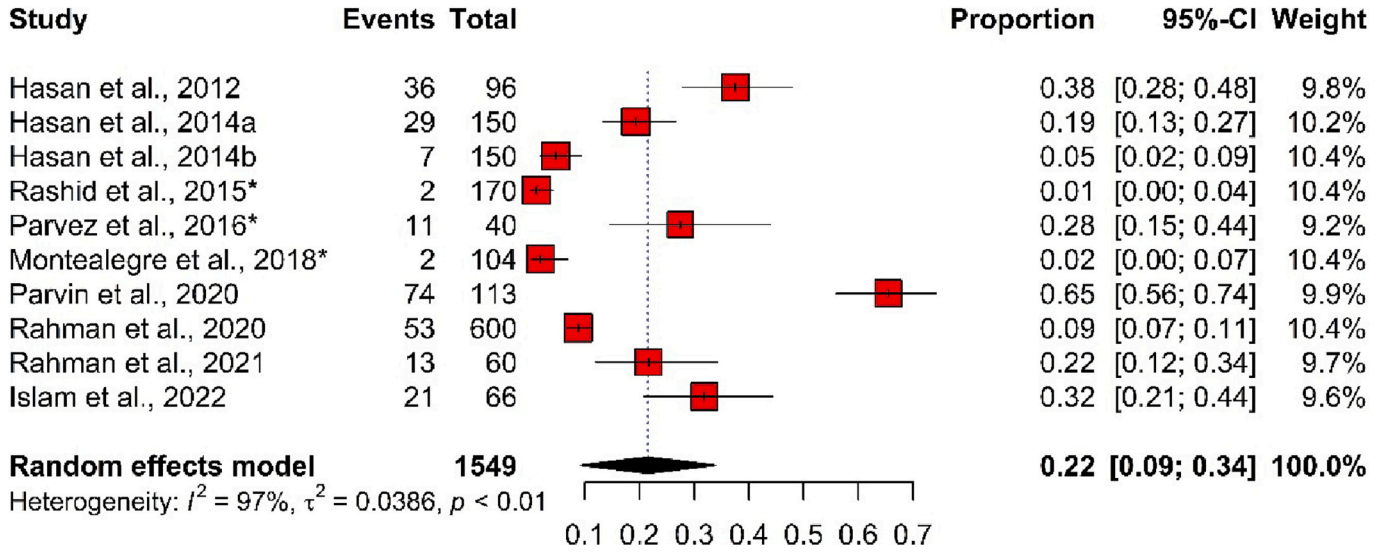

Fig. 5. Forest plot depicting the prevalence of ESBL-producing *E. coli* isolated from animal samples in Bangladesh. The estimate of the prevalence was determined by combining the findings of ten separate studies by applying a random-effects model to the data. An I^2 value > 75% and a p-value < 0.05 were deemed statistically significant. The R program was used to analyse the data and generate the figure. Events = No. of positive ESBL-producing *E. coli* isolated from each study, Total = Sample size of each study, CI = Confidence interval, * = Study conducted with more than one sample category.

producing *E. coli* in environmental samples ranged between 4% (95% CI: 0%–13%) and 65% (95% CI: 46%–80%) (Fig. 6).

3.6. Prevalence of genes encoding ESBL-producing E. coli

A total of 13 types of genes conferring ESBL-producers were detected in *E. coli* isolated from humans, animals, and environments. The ESBL gene bla_{TEM-1} showed the highest prevalence (37.5%), followed by bla_{CMY} (34.6%), $bla_{CTX-M-1}$ (20.7%), $bla_{CTX-M-15}$ (16.1%), bla_{TEM} (12.3%), bla_{CTX-M} and bla_{OXA} (9.6%), bla_{OXA-1} (5.8%), bla_{ampC} (3.9%), bla_{SHV} (3.8%), bla_{CMY-2} (2.3%), $bla_{CTX-M-14}$ (1.3%), and $bla_{CTX-M-9}$ (0.3%) (Table 2).

3.7. Epidemiological important clones

Seven out of 36 included articles recorded different clones ($n = 39$) where the *E. coli* clone ST131 was predominantly found in the included studies (5/7). The clinically relevant clone ST10 and ST48 were also reported in ESBL-producing *E. coli*. Khan et al. [47] and Hasan et al. [34] detected 17 and 11 types of *E. coli* clones, respectively. Also, *E. coli* clones were found in all of the sample categories (humans, animals, and environments) (Table 3).

4. Discussion

ESBL-producing *E. coli* strains have been identified as a prominent multidrug-resistant pathogen that have been linked to serious infections acquired in hospitals and communities all over the world. The treatment of *E. coli* infections has become particularly difficult because of the widespread emergence of ESBL-forming strains, which has reduced the number of effective antimicrobial agents available. Like in other countries, ESBL-producing *E. coli* strains are being regularly reported in humans, animals, and environments in Bangladesh. In this systematic review, we did a comprehensive analysis of data on the occurrence of ESBL-producing *E. coli* isolated from human, animal, and environmental samples in Bangladesh. We also focused on designing strategies to minimize the consequences of AMR in the multidisciplinary categories (humans, animals, and environments) by employing the One Health approach. To our knowledge, this is the first systematic review and meta-analysis in Bangladesh narrating the distribution of ESBL-producing *E. coli* in all the components of One Health to comprehend the AMR issue from a one-health perspective.

Table 2
Prevalence of ESBL genes in *E. coli* isolated from human, animal, and environmental samples in selected studies (published between 2010 and 2021) in Bangladesh.

Genes encoding ESBL	No. of studies	Total *E. coli* isolates	No. of positive ESBL genes (%)	Prevalence (%)	95% CI (%)
bla_{TEM}	14	2230	275	12.3	11.0–13.8
bla_{TEM-1}	3	344	129	37.5	32.6–42.7
bla_{CTX-M}	9	994	95	9.6	7.9–11.5
$bla_{CTX-M-1}$	9	1932	399	20.7	18.9–22.5
$bla_{CTX-M-9}$	5	1083	3	0.3	0.1–0.8
$bla_{CTX-M-14}$	2	151	2	1.3	0.2–4.7
$bla_{CTX-M-15}$	8	1184	191	16.1	14.2–18.3
bla_{SHV}	14	1993	76	3.8	3.1–4.8
bla_{CMY}	1	55	19	34.6	23.4–47.8
bla_{CMY-2}	2	684	16	2.3	1.5–3.8
bla_{OXA}	5	302	29	9.6	6.8–13.5
bla_{OXA-1}	7	1415	82	5.8	4.7–7.1
bla_{ampC}	4	762	30	3.9	2.8–5.6

Here, ESBL = Extended-spectrum beta-lactamase, CI = Confidence interval.

4.1. Prevalence of E. coli in humans, animals, and environments

The present study showed a high pooled prevalence of *E. coli* in humans, animals, and environments, reporting *E. coli* in >50% of the multidisciplinary samples. Previously, Bastidas-Caldes et al. [11] conducted a similar type of systematic review and meta-analysis and reported *E. coli* in 17.2% of the samples from humans, animals, and environments in South America, which is lower than our present study. The discrepancies in the prevalence of *E. coli* might be due to differences in geographical characteristics (e.g., location, temperatures, humidity, etc.), sample size, types, study period, and others. This systematic review showed that *E. coli* was isolated from diversified types of samples, e.g., urine, blood, pus, swabs from different organs (human samples), feces, cloacal swabs, meat or meat swabs (animal samples), and wastewater, sewage, and fecal sludge (environmental samples). The presence of *E. coli* in humans, animals, and environments shows a significant concern for a wide range of health communities because these isolates have the potential to be transferred from one component to another and vice versa. However, the objective of this study was not to determine the presence of *E. coli* isolates in humans, animals, and/or environments. The main purpose of the present study was to evaluate the prevalence of ESBL-producing *E. coli* in humans, animals, and environments, which has been discussed in detail later.

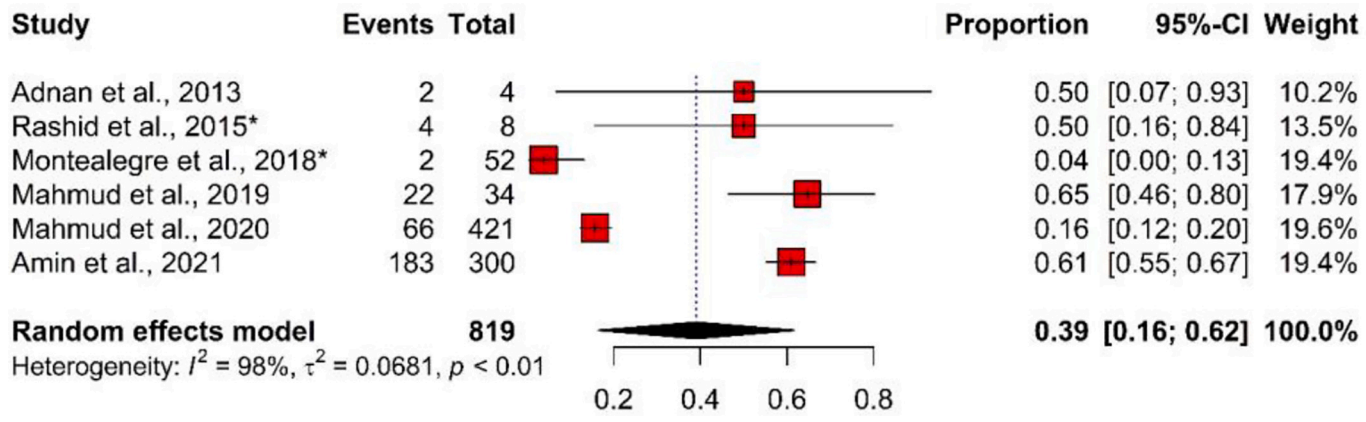

Fig. 6. Forest plot depicting the prevalence of ESBL-producing *E. coli* isolated from environmental samples in Bangladesh. The estimate of the prevalence was determined by combining the findings of six separate studies by applying a random-effects model to the data. An I^2 value > 75% and a p-value < 0.05 were deemed statistically significant. The R program was used to analyse the data and generate the figure. Events = No. of positive ESBL-producing *E. coli* isolated from each study, Total = Sample size of each study, CI = Confidence interval, * = Study conducted with more than one sample category.

Table 3
Sequence types (STs) clones found in *Escherichia coli* isolated from human, animal, and environmental samples in selected studies (published between 2010 and 2021) in Bangladesh.

Study ID	Study period	Sample categories	Sample types	Sequence types (STs)
Hasan et al. [30]	2009	Wild ducks, ducks, chickens, geese	Cloacal swabs, feces	ST131, ST405, ST448, ST648, ST744
Hasan et al. [34]	2010	Gull	Feces	ST10, ST48, ST131, ST345, ST349, ST648, ST853, ST1727, ST2687–2689
Hasan et al. [35]	2011	Pigeons	Cloacal swabs	ST1408, ST3489–92
Rashid et al. [41]	2010	Open Bill Stork, Environment	Feces, river water	ST10, ST46, ST156, ST2689, ST4016
Begum and Shamsuzzaman [43]	2014	Humans	Urine	ST131
Khan et al. [47]	2014–15	Humans	Urine, pus, swab of wound, vaginal, throat	ST38, ST73, ST88, ST101, ST127, ST131, ST155, ST167, ST224, ST405, ST410, ST466, ST754, ST851, ST1623, ST2104, ST2659, ST2851, ST6682
Jain et al. [58]	2019	Humans	Urine, sputum	ST131

4.2. ESBL-producing E. coli from humans, animals, and environments

In this study, the prevalence of ESBL-producing *E. coli* isolated from humans, animals, and environments was estimated to be 21% across all of Bangladesh, which is similar to the estimates for Latin America (23.2%) [62] and Europe (17.2%) [62], but lower than those reported for South Asia (33%) [9], the Asia-Pacific region (38.2%) [63], and Africa (40.4%) [62], and higher than the estimates for North America (9.8%) [62] and South America (3%) [11]. The variations in the prevalence of ESBL-producing *E. coli* might be due to differences in geographical properties, sample categories and types, sample size, identification methods, study periods, etc. In addition, there may be a correlation between the high population density, the scarcity of healthcare resources, and the lack of established antimicrobial stewardship programs in Bangladesh, all of which contribute to the region's disproportionately high incidence of these infections. Islam et al. [9] also conducted a systematic review and meta-analysis, reporting 35% ESBL-producing *E. coli* in Bangladesh, however, they focused only on humans, excluded those studies that incorporated non-human specimens (e.g., animals, foods, environments, etc.). But in this systematic review and meta-analysis, we extracted data on ESBL-producing *E. coli* isolated from all the One Health components.

In this study, the pooled prevalence of ESBL-producing *E. coli* from humans, animals, and environments was 17%, 22%, and 39%, respectively, which is comparable to a previous study [11] that reported ESBL-producing *E. coli* in human (2.2%), animal (21.4%), and environmental (12.6%) samples. The presence of ESBL-producing *E. coli* in animals and environments poses a serious health risk because it can be transmitted to humans through contact with animals and contaminated environmental components or through consumption of contaminated animal products or environmental elements. Moreover, carriers, who are otherwise healthy, are a significant reservoir for the transmission of beta-lactamases and, as a result, play a role in disseminating the bacteria to other populations or environments. The epidemiology of bacterial resistance in human populations may reveal a previously unknown pattern if further studies include surveillance at these levels [11].

Studies that were part of the One Health initiative were considered multidisciplinary because they analyzed samples from multiple interfaces, including human-animal, animal-environment, environment-human, and human-animal-environment, respectively. This review only reported on three cross-disciplinary studies (8.3%; 3/36), including human-animal, animal-environment, and human-animal-environment-related studies. The small number of multidisciplinary studies was also reported in other systematic reviews conducted globally [11,64,65]. As Bangladesh and other regions of the world are struggling to conduct their research using One Health approaches, the health authorities should take initiatives to combat the consequences of ESBL. For example, the World Health Organization suggests international cooperation to implement multi-sectoral action plans, which could help countries like Bangladesh and other parts of the world use "One Health" approaches in their experiment designs [66].

4.3. ESBL genes in E. coli isolated from humans, animals, and environments

This systematic review recorded that the ESBL genes bla_{TEM} and $bla_{CTX\text{-}M}$ genes were predominantly found among *E. coli* isolated from humans, animals, and environments in Bangladesh, which is supported by the previous studies [67–69]. These genes are typically found on the same large plasmids as the determinants of resistance that cause the bacteria to be resistant to multiple classes of antimicrobials [70]. Moreover, this review showed a high prevalence of the $bla_{CTX\text{-}M\text{-}1}$ and $bla_{CTX\text{-}M\text{-}15}$ genes in *E. coli* isolates from multidisciplinary samples, which has serious public health implications, because these types of genes are the predominant ESBL genes in humans [71]. This study also reported the presence of CTX-M-9-like enzymes ($bla_{CTX\text{-}M\text{-}9}$ and $bla_{CTX\text{-}M\text{-}14}$) in humans, animals, and environments, though these genes are directly or indirectly linked with animals [72]. In this systematic review, we found that two or more types of CTX-M type ESBLs co-existed in several studies, which indicates a serious issue in the treatment of infectious diseases caused by *E. coli* isolates. Since there are so many homologous regions between CTX-M strains, recombinant enzymes are a distinct possibility in a world where multiple CTX-M species coexist [73]. We hypothesize that the presence of multiple CTX-M types of genes in the isolates may indicate that infections caused by these isolates may be more challenging to treat due to the increased likelihood of ESBL expression occurring phenotypically [67]. According to the present study, other important ESBL genes, e.g., OXA, SHV, CMY, and ampC, were detected in animals, humans, and environments in Bangladesh, which also indicates a serious threat to health communities. The identification of ESBL genes in animals raises concerns about the environmental dissemination of the pathogen, which in turn could contribute to its transmission to farm workers and the wider community. Furthermore, the presence of ESBL genes in the environment has demonstrated the significance of these genes' spread in humans and animals, and vice versa.

4.4. Epidemiological important clones related to ESBL-producing E. coli

In this study, we found that seven out of 36 studies reported 39 types of *E. coli* clones in humans, animals, and environments in Bangladesh. Among them, the clone ST131 was predominantly (5/7) detected. ST131 is a highly virulent pathogenic clone of the extraintestinal pathogenic *E. coli* subgroup [74]. This type of clone is widely distributed in ESBL-producing *E. coli* around the globe [75–77]. The detection of this pandemic ST131 clone in ESBL-producing *E. coli* in humans, animals, and environments in Bangladesh is worrisome. The ST131 clone containing *E. coli* isolates are deemed to be highly pathogenic because of the variety of infections they produce in both community and hospital settings and the high number of genes linked with virulence that they carry

[78]. In addition, these clones are widely recognized as a significant source of plasmids harboring genes for resistance to several antimicrobial agents, including ESBL-encoding genes bla_{TEM}, bla_{CTX-M}, and bla_{SHV} [79]. The presence of other epidemiologically important *E. coli* clones in humans, animals, and environments indicates a serious public health issue. The issue of the rapid and continued existence of international high-risk clones in ESBL-producing *E. coli* at the multidisciplinary interface (humans, animals, and environments) needs to be viewed as a One Health challenge in Bangladesh.

4.5. Possible transmission pathways of ESBL-producing E. coli among One Health components

Although AMR is a concern for human health, this phenomenon has its origins at the interface between humans, animals, and the environment. As a result, resistant genes or bacteria find their way into the human food chain. There are many different ways that ESBL-producing *E. coli* can be transmitted. Animals, inanimate objects, and environments can directly and indirectly spread ESBL-producing *E. coli* and their related resistance genes to humans, as well as vice versa. Hospital communities are directly associated with the distribution of ESBL-producing *E. coli* to humans and environments via human-to-human transmission and contaminated sewage or water supplies, respectively. Wild birds can pick up ESBL-producing *E. coli* from their surroundings (especially surface-contaminated water) and act as vectors or transmitters of these organisms to humans and animals. Contaminated environmental components (e.g., water, food sources, etc.) may also directly transfer ESBL-producing *E. coli* to humans and animals through consumption of wastewater, foods, bathing, and others. Animals may also be responsible for the transmission of ESBL-producing *E. coli* to humans via direct contact and/or the food supply chain. Humans may contaminate animals and environments with ESBL-producing *E. coli* via direct contact with animals and transferring fecal sludge or waste to the environment. Fig. 7 depicts the possible transmission pathways of ESBL-producing *E. coli* to humans from various components of One Health process, as well as vice versa.

4.6. Mitigation of AMR consequences using One Health perspective approach

When it comes to global health issues, AMR is the issue that best exemplifies the One Health approach. Because of the imprudent and disproportionate use of antibiotics in a variety of fields, AMR is connected to all three components (humans, animals, and environments) of

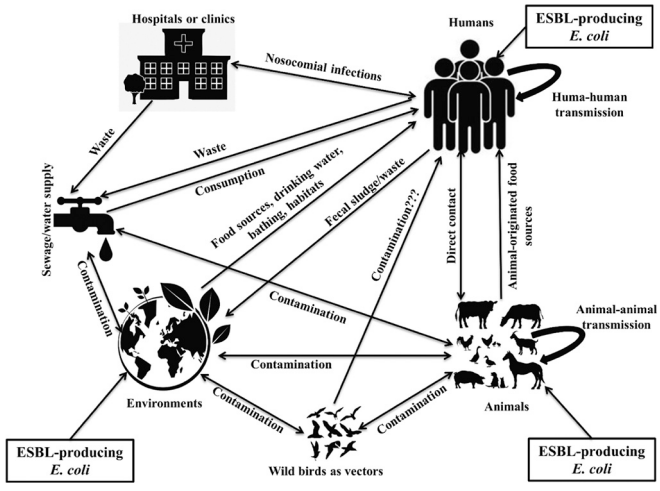

Fig. 7. Possible transmission dynamics of ESBL-producing *E. coli* and their associated genes into humans via One Health components and vice versa.

One Health [80]. The approach to One Health taken in the WHO Global Action Plan is pertinent and in line with the observations that have been made in other local and global action plans. A lot of work remains, however, until a comprehensive One Health plan is implemented on a national and international scale to mitigate AMR consequences [81]. As a result, the One Health approach is now fully incorporated into international initiatives to combat AMR. The following are some of the key strategies that the One Health approach recommends for combating AMR:

- It is imperative that both national and global surveillance systems be put in place to detect the emergence of antimicrobial-resistant and pathogenically important microbial hazards in One Health components. AMR surveillance entails the following stages: (1) data collection (including information on antibiotic use and its effects after it reaches consumers); (2) data integration, analysis, and interpretation; and (3) decision-making and the subsequent rollout of any necessary corrective measures based on the results of the surveillance (Fig. 8).
- The development of regulation in antimicrobial use and infection control in multiple sectors should be highlighted by a rigorous surveillance system.
- A public-awareness program should be implemented to improve knowledge among people about the dangers of misuse and excessive use of antimicrobial agents. It is possible to lower the number of prescribed antimicrobials by conducting successful public education campaigns.
- Expert veterinarians, human physicians, and environmental specialists must approve the use of any antimicrobial agents at any level. Without their consultation and approval, the use of all antimicrobial agents should be prohibited.
- The research, development, and widespread implementation of vaccines and alternative treatments (via vaccines, probiotics, bacteriophages, etc.) should be encouraged.
- Sanitation efforts at any level of the One Health program should be boosted in order to curb the spread of diseases, especially infectious diseases.

5. Limitations

Only peer-reviewed original articles were used in our systematic review. Our review excluded review articles, preprints, or theses that might have important information on ESBL-producing *E. coli*. Moreover, we had to exclude several peer-reviewed original articles because of the exclusion criteria. There is also an important note that even though the included articles were all judged to be of high quality based on their respective evaluation results, it is possible that a few of them appeared in predatory journals. Studies included in this review are trustworthy, and we base our conclusions not on the prestige of the journal in which they appeared but on the merits of the research presented therein.

6. Conclusion

As we know, this is the first systematic review and meta-analysis, reporting ESBL-producing *E. coli* isolated from all One Health components. This review reported a high prevalence of ESBL-producing *E. coli* in humans, animals, and environments. ESBL-producing *E. coli* in Bangladesh harbored a wide range of enzyme variants that are associated with ESBLs, including the clinically important ESBL TEM and CTX-M enzymes. The three most epidemiologically important clones, ST10, ST48, and ST131, were also detected in ESBL-producing *E. coli* isolated from humans, animals, and environments. The presence of ESBL-producing *E. coli*, their representative genes, and epidemiologically important clones in human, animal, and environmental samples indicates a serious issue in all the health communities in Bangladesh. The information gleaned from this meta-analysis can serve as the foundation

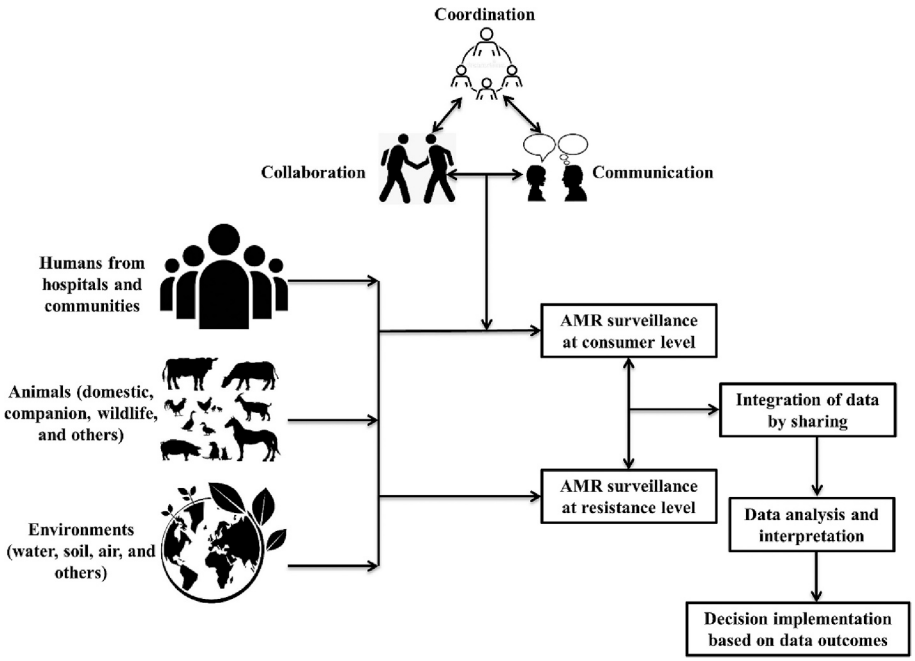

Fig. 8. A framework of multidisciplinary surveillance program to combat AMR consequences in different components of One Health (humans, animals, and environments).

for future monitoring initiatives that will significantly reduce potential scathing points in the transmission chain. Moreover, this systematic review emphasized how important it is to have complete AMR surveillance in Bangladesh to find out the exact scenario of ESBL-producing *E. coli* in humans, animals, and environments, and to speed up support for antimicrobial stewardship programs in Bangladesh. Finally, the One Health concept should be implemented in hospital communities, animal farms, and waste management plants to find out the transmission pathways of ESBL-producing *E. coli*, their resistant enzymes, and representative resistant genes. Multisectoral and multidisciplinary collaborations would be crucial to fulfill One Health principles and minimize the AMR consequences.

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Ethical approval

Not applicable.

Declaration of Competing Interest

The author reports no conflicts of interest in this work.

Data availability

Data will be made available on request.

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